Attached to this response is Werle et al. Werle (published in 2004) provides evidence, that the antibody IIIF10, i.e. an antibody according to the present invention that is specifically directed against the epitope 52-60 of uPAR, is not only used as a relevant marker for the prognosis of breast cancer carcinoma but also as significant prognostic factors for patients with non-small cell lung cancer. The data presented in Werle show that the antibody IIIF10 has a strong prognostic impact in the discrimination of patient collectives with NSCLC. Please see the following parts of Werle:

Page 4148, left-hand column, last part of the first paragraph, which states that "PAI-1 and uPAR (IIIF10) add independent prognostic information with regard to established clinical and histomorphological factors in NSCLC".

Page 4157, left-hand column, third paragraph and fourth paragraph, last sentence, which states that "PAI-1 and uPAR (IIIF10) remained the best independent prognostic factors for patients with NSCLC (Table VIII)".

Page 4158, right-hand column, third paragraph, which states that "PAI-1 and uPAR measured by mAb IIIF10 have a very strong independent prognostic impact".

Page 4159, left-hand column, first paragraph, which states that "PAI-1 and uPAR (IIIF10) proved to be independent prognostic factors, enabling better prognostic discrimination together with established clinical and histopathological factors".

Regarding Figure 10 in the present application, this figure shows the prognostic relevance of the uPAR antibody content in 203 breast cancer patients. In particular, Figure 10 shows the disease-free survival in the patients who were examined. The uPAR antigen was measured with three different ELISA systems in the patients (Figures 10a, 10b, and 10c respectively). Only when HU277 was used as a capture antibody

and IIIF10 was used as a detection antibody (Figure 10a) in an Elisa system, could the patients be separated into groups with good or bad prognosis. The differences between these two groups are statistically significant (p= 0.0015). The groups were discriminated by assigning all patients with a value of > 3.33 ng/mg to the group with a worse prognosis for the course of the disease and all patients with a value of < 3.33 ng/mg to the group with better prognosis for the course of the disease. Thus, the value of 3.33 ng/mg does indeed represent a cut-off value. Attached to this response is the publication Kotzsch et al., which further supports the data provided in the present application. In particular, Figure 5 of Kotzsch et al. confirm the results of Figure 10 of the present application.

Therefore, the present invention for the first time discloses that the detection of uPAR measured by antibodies directed against epitope 52-60 of uPAR provides a relevant prognostic means for the course of a malignant disease. In fact, it was surprisingly found that by using three ELISA systems, which all measure the same antigen, only one (the one wherein 111E10 is used as detecting antibody) enables the prognosis of a patient collective. This is due to the special characteristics of the antibody 111E10, which is specifically directed to epitope 52-60 of uPAR. The prognostic relevance of uPAR regarding breast cancer is clearly shown by the data in the present application and the prognostic relevance of uPAR regarding non-small cell lung cancer is shown in Werle. In view of the fact that the prognostic relevance of uPAR has been shown for these two unrelated cancers, applicants contend that one skilled in the art would reasonably expect uPAR to be a relevant prognostic means for the course of a malignant disease and request that this rejection be withdrawn.

Applicants respectfully submit that all of claims 30-35 are now in condition for allowance. If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

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